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09/380,447	09/01/1999	Sachdev S. Sidhu	P1581R2	2633

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EXAMINER

TRAN, MY CHAU T

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 03/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/380,447

Applicant(s)

SIDHU ET AL.

Examiner

MY-CHAU T. TRAN

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 November 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3,4,7-9,11,12,29-33,44-49 and 52-58 is/are pending in the application.
- 4a) Of the above claim(s) 29,48,49 and 52-54 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3,4,7-9,11,12,30-33,44-47 and 55-58 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 01 September 1999 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>11/18/05 & 2/26/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/18/2005 has been entered.

Application and Claims Status

2. Applicant's amendment and response filed 11/18/2005 is acknowledged and entered. Claims 1 and 31 have been amended. Claims 55-58 have been added.
3. The amendment filed on 08/22/2005: cancelled claim 42 and amended the specification to note the correct priority of this application.
4. The amendment filed on 6/14/2004: cancelled claims 34-41, 43, 50, and 51; amended claims 31; and added claims 52-54.
5. The amendment filed on 2/26/2004: cancelled claims 2, 5, 6, 10, and 13-28; amended claims 1, 11, and 12; and added claims 29-51.
6. Claims 1, 3, 4, 7-9, 11, 12, 29-33, 44-49, and 52-58 are pending.

Election/Restrictions

7. The instant species election requirement is still in effect as there is no allowable generic or linking claim. Applicant has elected the following species for the elected invention (Claims 1, 3, 4, 7-9, 11, 12, 29-33, 44-49, and 52-58) in the reply filed on 11/02/2004:

- a. For the single specific species of a major coat protein, applicant elected a filamentous phage of gp VIII, i.e. wild type M13 with the sequence of SEQ ID NO. 2.
- b. For the single specific species of variant of the major coat protein, applicant elected variant of the major coat protein, i.e. wild type M13 with the sequence of SEQ ID NO. 2, wherein the amino acid and its position are as follows: Position No./Amino Acid: 1/D, 2/K, 3/S, 4/E, 5/K, 6/F, 7/S, 8/R, 9/D, 11/Y, 12/E, 13/A, 14/L, 15/E, 16/D, 17/I, 18/I, 19/T, 20/N, 21/L, 22/F, 23/F, 24/L, 25/L, 26/G, 27/T, 28/V, 29/Y, 30/V.
- c. For the single specific species of heterologous protein, applicant elected an antibody or fragment thereof.
- d. For the single specific species of linking peptide, applicant elected SEQ ID NO. 110.
- e. For the single specific species of target, applicant elected erb 2.

8. Applicant's election of species in the reply filed on 11/2/2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

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9. Claims 29, 48, 49, and 52-54 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to *non-elected species*, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/2/2004.

10. Claims 1, 3, 4, 7-9, 11, 12, 30-33, 44-47, and 55-58 are under consideration in this Office Action.

Priority

11. This instant application is a 371 of PCT/US99/16,596 filed 7/22/1999, which claims benefit to four provisional applications. They are 60/094,291 filed 07/27/1998, 60/103,514 filed 10/08/1998, 60/133,296 filed 05/10/1999, and 60/134,870 filed 05/19/1999. However, the instant claims 1, 3, 4, 7-9, 11, 12, 30-33, 44-47, and 55-58 are granted the benefit of priority for 60/103,514 filed 10/08/1998 and 60/134,870 filed 05/19/1999 under 35 U.S.C. 119(e).

12. It is noted in the response filed 08/22/2005 that applicant also requested for a corrected filing receipt with regard to the claimed benefit for the four provisional applications. The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of Office records to reflect the claimed benefit for the four provisional applications as corrected.

Information Disclosure Statement

13. The information disclosure statement (IDS) filed on 11/18/2005 has been reviewed, and its references have been considered as noted on PTO-1449 form(s). In addition, the references of US Patents 6,054,312 and 6,190,908 B1 were considered by the examiner for the IDS filed 02/26/2004 and it is noted that the PTO-1449 form mailed to the applicant was not properly signed and dated by the examiner. The properly signed and dated PTO-1449 form for the IDS filed 02/26/2004 is enclosed, and the examiner apologizes for the inconvenience.

14. Please note: Applicant's *specifically* elected species of a fusion protein, which comprises a variant of filamentous phage of gp VIII, i.e. wild type M13 with the sequence of SEQ ID NO. 2 wherein its amino acid variant at the following position are as follows: (Position No./Amino Acid) 1/D, 2/K, 3/S, 4/E, 5/K, 6/F, 7/S, 8/R, 9/D, 11/Y, 12/E, 13/A, 14/L, 15/E, 16/D, 17/I, 18/I, 19/T, 20/N, 21/L, 22/F, 23/F, 24/L, 25/L, 26/G, 27/T, 28/V, 29/Y, 30/V; a linking peptide of SEQ ID NO. 110; and an antibody that binds to erb 2 (see paragraph 6 above). The elected species of a fusion protein was searched and was not found in the prior art. Also, see MPEP § 803.02 (emphasis added):

On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. ***The prior art search, however, will not be extended unnecessarily to cover all nonelected species.*** Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action >can be< made final >unless the examiner introduces a new ground of rejection that is neither necessitated by applicant's amendment of the claims nor based on information submitted in an information disclosure statement filed during the period set forth in 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p). See MPEP § 706.07(a)<. Amendments submitted after the final rejection further restricting the scope of the

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claim may be denied entry >if they do not comply with the requirements of 37 CFR 1.116. See MPEP § 714.13.

Thus the search was expanded to non-elected species, which *were* found in the prior art; see rejections below.

Claim Rejections - 35 USC § 112

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 1, 3, 4, 7-9, 11, 12, 30-33, 44-47, and 55-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant claim 1 recites a fusion protein, i.e. a product. Structurally, the product comprises a heterologous polypeptide fused to at least a portion of a variant of a wild type major coat protein of a virus. The variant of a wild type major coat protein of a virus is selected from the group consisting of a filamentous phage, a lambda phage, a Baculovirus, a T4 phage and a T7 phage.

As claimed, the variant is a broad genus wherein there is no core structure, i.e. there is no identification of any particular portion of the structure that must be conserved for the instant

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claimed variant. Although the claimed variant also claimed that it is from the wild type major coat protein of a virus, i.e. phage display systems, that include the phage display systems of a filamentous phage, a lambda phage, a Baculovirus, a T4 phage and a T7 phage, this limitation is not sufficient to provide a core structure since there is a substantial variation within the genus of these 'different' phage display systems (i.e. a filamentous phage, a lambda phage, a Baculovirus, a T4 phage and a T7 phage) such that the structure of the wild type major coat proteins among these 'different' phage display systems are structurally distinct from each other, i.e. there is no structural nexus among these wild type major coat proteins of these 'different' phage display systems. Therefore, the claimed variant is a broad genus wherein there is no core structure.

The instant specification disclosure does not sufficiently teach the broad genus for the claimed variant of wild type major coat protein of phage display systems that include the phage display systems of a lambda phage, a Baculovirus, a T4 phage and a T7 phage. The instant specification disclosure provides the definition of the terms "variant" and "mutant" (see pg. 19, lines 16-35), the listing of phage display systems such as filamentous phage, lambda phage, Baculovirus, T4 phage and T7 phage (see pg. 36, lines 22-37; pg. 43, lines 13-14), and the statement that the wild type major coat protein of these phage display systems (i.e. a lambda phage, a Baculovirus, a T4 phage and a T7 phage) can be mutated to form the variant of a wild type major coat protein (see pg. 43, lines 14-19). The instant specification description is directed to the variant of wild type major coat protein of the filamentous phage, i.e. the major coat protein VIII of a filamentous phage (see pg. 39, line 1 thru pg. 43, line 12). The instant sequence listing discloses the wild type major coat protein of the filamentous phage, i.e. SEQ ID NO. 2, 3, 4, 5, 6, 7, and 8, which are also claimed in claim 31. The specification examples are drawn to the

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method of making the variant of wild type major coat protein VIII of the filamentous phage (see pgs. 72-74, Example 10-12; pgs. 80-83, Examples 24-25) and the method of using the variant of wild type major coat protein VIII of the filamentous phage (see pgs. 74-77, Example 13-21; pgs. 84-85, Example 26). These disclosure clearly does not provide an adequate representation regarding the broad genus for the claimed variant of wild type major coat protein of phage display systems that include the phage display systems of a lambda phage, a Baculovirus, a T4 phage and a T7 phage because there is a substantial variation within the genus of these 'different' phage display systems, i.e. a filamentous phage, a lambda phage, a Baculovirus, a T4 phage and a T7 phage, such that the structure of the wild type major coat proteins among these 'different' phage display systems are structurally distinct from each other, i.e. there is no structural nexus among there wild type major coat proteins of these 'different' phage display systems. Consequently, the instant specification disclosure does not sufficiently teach the broad genus for the claimed variant of wild type major coat protein of phage display systems that include the phage display systems of a lambda phage, a Baculovirus, a T4 phage and a T7 phage.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present for the claimed variant is their functions for binding and displaying a heterologous polypeptide. There is not even identification of any particular portion of the structure that must be conserved among the claimed variant, i.e. no core structure. Although the claimed variant also claimed that is from

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the wild type major coat protein of a virus, i.e. phage display systems, that include the phage display systems of a filamentous phage, a lambda phage, a Baculovirus, a T4 phage and a T7 phage, this limitation is not sufficient to provide a core structure since there is a substantial variation within the genus of these 'different' phage display systems, i.e. a filamentous phage, a lambda phage, a Baculovirus, a T4 phage and a T7 phage, such that the structure of the wild type major coat proteins among these 'different' phage display systems are structurally distinct from each other, i.e. there is no structural nexus among there wild type major coat proteins of these 'different' phage display systems. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus for the claimed variant.

Thus, the specification does not teach the broad genus for the claimed variant of wild type major coat protein of phage display systems that include the phage display systems of a lambda phage, a Baculovirus, a T4 phage and a T7 phage.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See page 1116.).

With the exception of the variant of wild type major coat protein of a filamentous phage, i.e. the coat protein VIII of a filamentous phage, disclosed by the specification, the skilled artisan cannot envision the instant claimed fusion protein comprising a heterologous polypeptide and

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any variant of any wild type major coat protein of phage display systems that includes the display systems of a lambda phage, a Baculovirus, a T4 phage and a T7 phage. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for making it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

In the present instance, the specification does not teach instant claimed fusion protein comprising a heterologous polypeptide and any variant of any wild type major coat protein of phage display systems that includes the display systems of a filamentous phage, a lambda phage, a Baculovirus, a T4 phage and a T7 phage. Therefore, only the fusion protein comprising a heterologous polypeptide and the variant of wild type major coat protein of a filamentous phage, specifically the coat protein VIII, but not the full breadth of the claimed product meet the written description provision of 35 U.S.C 112, first paragraph.

17. The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

18. Claims 3 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claim 3 recites the limitation of "the phage" in line 1. There is insufficient antecedent basis for this limitation in claim 1. Claim 1 recites a Markush group regarding the type of variant of a wild type major coat protein of virus, i.e. '*a virus selected from the group consisting of a filamentous phage, a lambda phage, a Baculovirus, a T4 phage and a T7 phage*'.

b) The phrase "the major coat protein" of both claims 3 and 44 vague because it is unclear if it is referring to the '*variant of a wild type major coat protein*' or the '*wild type major coat protein*'. Consequently, the phrase "the major coat protein" of both claims 3 and 44 vague and both claims 3 and 44 are rejected under 35 U.S.C. 112, second paragraph.

c) Claim 4 recites the limitation of "the major coat protein" in line 1. There is insufficient antecedent basis for this limitation in claim 1. Claim 1 recites '*a wild type major coat protein*'.

Claim Rejections - 35 USC § 102

19. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

20. Claims 1, 8, 9, 11, 12, 30, 46, and 47 are rejected under 35 U.S.C. 102(e) as being anticipated by Larocca et al. (US Patent 6,451,527 B1; *effective filing date of 08/29/199*).

The instant invention recites a fusion protein, i.e. a product. Structurally, the product comprises a heterologous polypeptide fused to at least a portion of a variant of a wild type major coat protein of a virus. The variant of a wild type major coat protein of a virus is selected from the group consisting of a filamentous phage, a lambda phage, a Baculovirus, a T4 phage and a T7 phage.

Larocca et al. disclose a genetic package display system and the method of using it (see e.g. Abstract; col. 2, lines 14-63; col. 3, lines 3-19). The genetic package display system comprises a ligand fused to the phage coat protein (see e.g. col. 3, lines 39-40; col. 4, line 64-65; col. 9, lines 57-65; fig. 1B). The ligand includes foreign protein, peptides, antibodies, or cDNA (refers to instant claimed heterologous polypeptide and instant claims 8, and 46)(see e.g. col. 4, line 64-65; col. 5, line 54 thru col. 6, line 62; col. 9, lines 57-65). In addition the ligand can bind to target such as erbB3 (refers to instant claim 47)(see e.g. col. 11, lines 18-30). The phage coat protein comprises a wild type major coat protein such as filamentous phage, lambda phage, and T4 phage (refers to instant claim 30)(see e.g. col. 4, line 66 thru col. 5, line 53) or mutant coat protein such as the mutant filamentous phage coat protein VIII (refers to instant claimed variant of a wild type major coat protein of a virus and the elected species of filamentous phage of gp VIII)(see e.g. col. 9, lines 36-44). The transformation of the genetic package display system uses host cell such as bacteria host cell (refers to instant claims 9 and 11)(see e.g. col. 7, lines 15-22; col. 10, lines 46-63; col. 11, lines 1-17; col. 17, lines 1-31) and include viral replication system

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(refers to instant claim 12)(see e.g. col. 7, line 33 thru col. 8, line 6). Therefore, the genetic package display system of Larocca et al. anticipates the presently claimed fusion protein.

Claim Rejections - 35 USC § 103

21. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

22. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

23. Claims 1, 3, 8, 9, 11, 12, 30-32, 44, 46, and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Light, II et al. (US Patent 5,770,356) in view of Larocca et al. (US Patent 6,451,527 B1; *effective filing date of 08/29/199*).

The instant invention recites a fusion protein, i.e. a product. Structurally, the product comprises a heterologous polypeptide fused to at least a portion of a variant of a wild type major coat protein of a virus. The variant of a wild type major coat protein of a virus is selected from the group consisting of a filamentous phage, a lambda phage, a Baculovirus, a T4 phage and a T7 phage.

Light, II et al. disclose a fusion protein (see e.g. Abstract; col. 1, lines 13-17; col. 3, lines 31-38; col. 9, lines 3-5, and 32-35). The fusion protein comprises a heterologous polypeptide attached to the filamentous phage membrane coat protein, and the attachment is through a polypeptide linker at the carboxy terminus of the heterologous polypeptide (see e.g. col. 9, lines 3-5, and 32-35; col. 10, lines 13-34; col. 10, line 58 to col. 11, line 20). The filamentous phage includes phage such as M13, f1, and fd, and membrane coat protein include coat protein such as a gene VIII coat protein (see e.g. col. 10, lines 13-34; col. 13, lines 41-45; col. 22, line 50 thru col. 12). The expression vectors of the host cell encode the fusion protein (see e.g. col. 19, lines 6-41).

The fusion protein of Light, II et al. differs from the presently claimed invention by failing to disclose a variant major coat protein.

Larocca et al. disclose a genetic package display system and the method of using it (see e.g. Abstract; col. 2, lines 14-63; col. 3, lines 3-19). The genetic package display system comprises a ligand fused to the phage coat protein (see e.g. col. 3, lines 39-40; col. 4, line 64-65; col. 9, lines 57-65; fig. 1B). The ligand includes foreign protein, peptides, antibodies, or cDNA (refers to instant claimed heterologous polypeptide and instant claims 8, and 46)(see e.g. col. 4, line 64-65; col. 5, line 54 thru col. 6, line 62; col. 9, lines 57-65). In addition the ligand can bind to target such as erbB3 (refers to instant claim 47)(see e.g. col. 11, lines 18-30). The phage coat protein comprises a wild type major coat protein such as filamentous phage, lambda phage, and T4 phage (refers to instant claims 30 and 31)(see e.g. col. 4, line 66 thru col. 5, line 53) or mutant coat protein such as the mutant filamentous phage coat protein VIII (refers to instant claimed variant of a wild type major coat protein of a virus and the elected species of filamentous phage

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of gp VIII)(see e.g. col. 9, lines 36-44). In addition, the mutant coat protein increases transduction efficiency (refers to instant claim 32)(see e.g. col. 9, lines 36-44; especially col. 9, lines 40-44). The transformation of the genetic package display system uses host cell such as bacteria host cell (refers to instant claims 9 and 11)(see e.g. col. 7, lines 15-22; col. 10, lines 46-63; col. 11, lines 1-17; col. 17, lines 1-31) and include viral replication system (refers to instant claim 12)(see e.g. col. 7, line 33 thru col. 8, line 6).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to disclose a variant major coat protein as taught by Larocca et al. in the fusion protein of Light, II et al. One of ordinary skill in the art would have been motivated to disclose a variant major coat protein in the fusion protein of Light, II et al. for the advantage of providing a coat protein that allows for more rapid uncoating and increased transduction capacity (Larocca: col. 9, lines 40-44) since both Light, II et al. and Larocca et al. disclose filamentous phage wild type major coat protein such as M13, gene III, and gene VIII (Light, II: col. 10, lines 13-34; Larocca: col. 4, line 66 thru col. 5, line 1). Furthermore, one of ordinary skill in the art would have a reasonable expectation of success in the combination of Light, II et al. and Larocca et al. because the type of major coat protein use in the fusion protein would be a choice of experimental design and is considered within the purview of the cited prior art.

Therefore, the combine teachings of Light, II et al. and Larocca et al. do render the fusion protein of the instant claims *prima facie* obvious.

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24. Claims 1, 7-9, 11, 12, 30-32, 46, 47, 55, and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Larocca et al. (US Patent 6,451,527 B1; *effective filing date of 08/29/199*) in view of Li et al. (*J. Biol. Chem.*, **1993**, 268(7), pgs. 4584-4587).

The instant invention recites a fusion protein, i.e. a product. Structurally, the product comprises a heterologous polypeptide fused to at least a portion of a variant of a wild type major coat protein of a virus. The variant of a wild type major coat protein of a virus is selected from the group consisting of a filamentous phage, a lambda phage, a Baculovirus, a T4 phage and a T7 phage.

Larocca et al. disclose a genetic package display system and the method of using it (see e.g. Abstract; col. 2, lines 14-63; col. 3, lines 3-19). The genetic package display system comprises a ligand fused to the phage coat protein (see e.g. col. 3, lines 39-40; col. 4, line 64-65; col. 9, lines 57-65; fig. 1B). The ligand includes foreign protein, peptides, antibodies, or cDNA (refers to instant claimed heterologous polypeptide and instant claims 8, and 46)(see e.g. col. 4, line 64-65; col. 5, line 54 thru col. 6, line 62; col. 9, lines 57-65). In addition the ligand can bind to target such as erbB3 (refers to instant claim 47)(see e.g. col. 11, lines 18-30). The phage coat protein comprises a wild type major coat protein such as filamentous phage, lambda phage, and T4 phage (refers to instant claims 30 and 31)(see e.g. col. 4, line 66 thru col. 5, line 53) or mutant coat protein such as the mutant filamentous phage coat protein VIII (refers to instant claimed variant of a wild type major coat protein of a virus and the elected species of filamentous phage of gp VIII)(see e.g. col. 9, lines 36-44). In addition, the mutant coat protein increases transduction efficiency (refers to instant claim 32)(see e.g. col. 9, lines 36-44; especially col. 9, lines 40-44). The transformation of the genetic package display system uses host cell such as bacteria host cell (refers to instant claims 9 and 11)(see e.g. col. 7, lines 15-22; col. 10, lines 46-

63; col. 11, lines 1-17; col. 17, lines 1-31) and include viral replication system (refers to instant claim 12)(see e.g. col. 7, line 33 thru col. 8, line 6).

The fusion protein of Larocca et al. differs from the presently claimed invention by failing to disclose the amino acid substitution for the variant of a wild type major coat protein.

Li et al. disclose mutant M13 coat protein (see e.g. Abstract; pg. 4584, right col., lines 6-37; pg. 4585, fig. 1). The mutagenesis comprises randomized oligonucleotides annealed to either the wild type major coat protein of M13 or the mutant of the wild type major coat protein of M13 and the transformation step use *E coli* as the host cell (see e.g. pg. 4584, right col., lines 40-69; pg. 4585, left col., lines 8-19). The amino acid substitution ranges from 2 to 13 and the site of the mutation is at residues numbers 22, 23, 24, 27, 28, 29, 30, 31, 32, 33, 36, 37, and 38 (see e.g. pg. 4584, right col., line 40 thru pg. 4585, left col., line 6; pg. 4585, left col., lines 19-47; pg. 4585, fig. 1).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to disclose the amino acid substitution for the variant of a wild type major coat protein as taught by Li et al. in the fusion protein of Larocca et al. One of ordinary skill in the art would have been motivated to disclose the amino acid substitution for the variant of a wild type major coat protein in the fusion protein of Larocca et al. for the advantage of providing a major coat protein with alter species distributions and protein-protein interaction within the transmembrane region (Li: pg. 4586, right col., lines 5-11) since both Larocca et al. and Li et al. disclose mutant filamentous phage major coat protein VIII (Larocca: col. 9, lines 40-44; Li: pg. 4585, fig. 1). Furthermore, one of ordinary skill in the art would have a reasonable expectation of success in the combination of Larocca et al. and Li et al. because Li et al. disclose the success

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of the amino acid substitution for the variant of a wild type major coat protein for use in mutagenesis (Li: pg. 4585, right col., lines 3-14).

Therefore, the combine teachings of Larocca et al. and Li et al. do render the fusion protein of the instant claims *prima facie* obvious.

Withdrawn Objection(s) and /or Rejection(s)

25. The rejection of claims 1, 3, 4, 7, 9, 11, 12, 30, 31, and 44 under 35 USC 102(b) as being anticipated by Light, II et al. (US Patent 5,770,356) has been withdrawn in light of applicant's amendments of claim 1.

26. The rejection of claims 1, 3, 4, 7-9, 11, 12, 30-33, and 44-47 under 35 USC 103(a) as being obvious over Light, II et al. (US Patent 5,770,356) and Marks et al. (US Patent 6,794,128 B2) has been withdrawn in view of applicant's amendments of claim 1.

Response to Arguments

27. Applicant's arguments with respect to claims 1, 3, 4, 7-9, 11, 12, 30-33, and 44-47 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

28. No Claims allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to My-Chau T. Tran whose telephone number is 571-272-0810. The examiner can normally be reached on Monday: 8:00-2:30; Tuesday-Thursday: 7:30-5:00; Friday: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

My-Chau T. Tran
February 27, 2006

